Remarks

In view of the above amendments and the following remarks, reconsideration of the outstanding office action is respectfully requested.

The applicants would like to thank Examiner Dickinson for the courtesy extended to the undersigned attorney during the telephone interview on February 18, 2009. The substance of the interview is addressed below.

Claims 8 has been further amended to delete the language "residues of" and to clarify that the material comprising tissue-reactive functional groups is the reaction product of recited reactants (i) and (ii). Descriptive support for these amendments appear in the paragraphs at page 11, lines 21-27; page 11, line 24 to page 12, line 9 (and Figure 2); page 12, lines 11-16 (and Figure 3); page 13, lines 4-19; page 15, lines 9-12; and Figure 5.

Claims 1-11, 13-44, 53, and 63-67 are pending, with claims 11, 31-44, 53, and 63-67 being withdrawn from consideration.

The rejection of claims 8-10 and 12-19 under 35 U.S.C. § 112 (first para.) for lack of written description is respectfully traversed.

On page 2 of the outstanding office action, the U.S. Patent and Trademark Office ("PTO") asserts that the specification fails to provide sufficient descriptive support for the claim language "material ... formed by derivatization of a polymer precursor," because (it is asserted) there are few representative examples and insufficient guidance is provided to what compounds are encompassed by the recited genus. Applicants respectfully disagree.

Claim 8 has been amended to recite that the material is the reaction product of reactants (i) and (ii) as recited. Reactant (i), the polymer precursor, comprises "two or more monomers, at least one of the monomers containing a carboxylic acid group or a group capable of being reacted with another material to form an acid functionality." In other words, structural features of a monomer subunit that forms the polymer precursor is presently recited in claim 8.

The description in the present application fully supports this recitation of structural features for the particulate material containing tissue-reactive functional groups. Classes of polymers which lend themselves to reaction with the reactant comprising a tissue-reactive functional group, reactant (ii), include those that contain carboxylic acid or alcohol functional groups. Commercially available polymers that may be used include polyvinylalcohol ("PVA"). The use of PVA-modified polymers is described at page 11, line 20 to page 12, line 9.

At page 12, lines 11-26, the specification clearly recites that a wide variety of monomers may be used to form the polymer precursor. These include *N*-vinyl-2-pyrrolidone, acrylic acid, vinyl acetate, vinyl acetic acid, mono-2-(methacryloyloxy)ethyl succinate, methacrylic acid, 2-hydroxyethyl methacrylate, 2-hydroxypropyl methacrylate, (polyethylene glycol) methacrylate or other monomers containing acid or alcohol functionality.

The present application also teaches at page 10, line 30, to page 11, line 19, that suitable tissue-reactive functional groups include those functional groups capable of reaction (under the conditions prevalent when the formulation is applied to tissue, i.e., in an aqueous environment and without the application of significant amounts of heat or other external energy) with functional groups present at the surface of the tissue. The latter class of functional group includes thiol and amine groups, and tissue-reactive functional groups therefore include groups reactive to thiol and/or amine groups. Examples include imido ester, p-nitrophenyl carbonate, N-hydroxysuccinimide (NHS) ester, epoxide, isocyanate, acrylate, vinyl sulfone, orthopyridyl-disulfide, maleimide, aldehyde, and iodoacetamide, although NHS ester is identified as preferred.

In view of the foregoing, it is submitted that a person of ordinary skill in the art would have recognized that the inventors of the present application had possession of the claimed invention at the time the application was filed. Therefore, the rejection of claims 8-10 and 12-22 for lack of written description is improper and should be withdrawn.

The rejection of claims 1-10, 12-16, 19-20, 28, and 29 under 35 U.S.C. §102(b) as anticipated by German Patent Application No. DE 35 02 998 to Schönwald et al. ("Schönwald") is respectfully traversed.

In maintaining this rejection, the PTO contends at page 3 of the office action that Example 1 of Schönwald specifically discloses ferrite particles in admixture with particles of poly (N-vinyl-2-pyrrolidone-co-acrylic acid) bearing N-hydroxysuccinimide esters. The PTO then cites U.S. Patent No. 6,329,115 to Yamashita ("Yamashita") as evidence that ferrite particles have the property of being cross-linkable. Applicants respectfully disagree, because Yamashita does not at all teach that the ferrite particles are "crosslinkable" within the meaning of the presented claims.

The cited portion of Yamashita recites as follows:

> Further, ferrite particles with a particle size of 100 μm were coated with a silicone resin, following by crosslinking, so that those silicone-resin-coated ferrite particles were prepared as the carrier particles.

Yamashita, at col. 31, lines 13-16. However, the reference to crosslinking in this context is to the crosslinking of a silicone resin precursor to coat the ferrite particles in silicone resin, not crosslinking of the ferrite particles themselves (i.e., one particle to another). Thus, Yamashita does not teach the crosslinking of ferrite particles.

For a material to be "polymerisable and/or crosslinkable," according to the present invention, it must be capable of polymerizing and/or forming covalent bonds between molecules (see page 8, lines 1-10 of the present application). Neither Schönwald nor Yamashita demonstrate that this is possible for the ferrite particles themselves.

In Schönwald, the ferrite particles are coated in plastic, and these plastic coated particles of ferrite cannot be considered to provide a synthetic crosslinkable material in particulate form. That is because they are already chemically crosslinked to tumour-specific antibodies or effect factors. During manufacture, functional groups on the plastic are converted into activated groups, e.g., NHS esters, that will react with functional groups on the antibodies or effect factors. Once the plastic-coated particles have been coupled to antibodies or effect factors, there are no longer activated groups available for crosslinking. If the plastic were partially crosslinked such that groups remained available for crosslinking, then the particles would surely be unsuitable for their intended purpose because they would adhere to non-targeted tissue and, thus, would not be able to travel through the body to accumulate on antibody-targeted tumor sites.

Yet a further distinction between the present claims and Schönwald is that the claims require two distinct particulate materials in admixture. The conjugated product disclosed in Schönwald does not contain two distinct particulate materials.

Schönwald is therefore deficient in at least two respects with the invention of claim 1. Because Schönwald does not teach or suggest each and every limitation of claim 1 (and claims dependent thereon), the rejection of claims 1-10, 12-16, 19-20, 28, and 29 as anticipated by Schönwald is improper and should be withdrawn. During the telephone interview, Examiner Dickinson agreed that the rejection as currently set forth would be withdrawn given these deficiencies.

The rejection of claims 1-4, 6-10, and 29-30 under 35 U.S.C. § 103(a) for obviousness over U.S. Patent No. 6,989,192 to Husemann et al. ("Husemann") is respectfully traversed.

The manufacture of adhesive tapes is described by Husemann in which a blend of polyacrylate hotmelt and polymer particles is applied to one or more backing materials,

and then a crosslinking reaction is initiated by thermal or UV radiation. These polymer particulates are added to the composition prior to curing to improve the cohesive properties of the adhesive. Due to the improved cohesion of this adhesive tape, it can be used for industrial applications involving high temperatures or high shearing loads (column 8, lines 42-46). The invention is said to be particularly suitable for the thermal crosslinking of acrylic hotmelts, a process that is usually difficult because the majority of crosslinking agents react during the actual hotmelt process (column 2, lines 3-7).

Applicants respectfully submit that claim 1 (and claims dependent thereon) would not have been obvious in view of Husemann for several reasons.

Firstly, a person of ordinary skill in the art would not even have considered looking at Husemann for assistance in making the present invention. The present invention is concerned with formulations that are suitable for application to internal tissue surfaces such as the surfaces of internal organs exposed during surgical procedures, including conventional and minimally invasive surgery. Conversely, Husemann refers to an improvement in standard polyacrylate pressure sensitive adhesives, which are known to the skilled person to have general industrial applicability and to be unsuitable for internal medical applications.

Secondly, Husemann does not teach or suggest a naturally occurring or synthetic polymerisable and/or cross-linkable material *in particulate form and in admixture with particulate material* comprising tissue-reactive functional groups as required by claim 1. Put simply, claim 1 recites an admixture of two particulate materials, and Husemann does not teach or suggest such an admixture. As noted above, Husemann teaches blending a pressure sensitive adhesive *melt* with polymer particles, and not an admixture of a polymerisable and/or cross-linkable material in particulate form with particulate material comprising tissue-reactive functional groups, as required by the present claims.

Despite this deficiency, the PTO at page 4 of the office action contends that the melt is prepared by "mixing *particles* of (a) acrylic acid and methacrylic acid derivatives with particles of (b) vinyl, acrylic and/or methacrylic monomers having a group X" (emphasis added). While the melt contains a monomer mixture of components (a) and (b), applicants respectfully submit that the PTO is incorrect in asserting that this mixture involves two particulate forms. This deficiency has already been demonstrated (above). Moreover, it is stated at column 1, lines 19-20 of Husemann that pressure sensitive adhesive polyacrylates are generally prepared *in solution* by free radical polymerization.

As discussed during the interview, the cited portion of Husemann concerning the free radical polymerization of components (a) and (b), at col. 5, lines 18-50, does not discuss a mixture of particulate material. Instead, Husemann describes carrying out this polymerization in a solvent with subsequent solvent removal (after polymerization) to form the melt.

It is stated at column 6, lines 19-20 that "[t]he polymerization may be conducted in the presence of one or more organic solvents and/or in the presence of water." In the examples (column 10) the solvent that is used is 1:1 acetone/special boiling point spirit 60/95. Husemann recites that the "preferred processes use as little solvent as possible" (column 6, lines 23-24), and that after polymerization has occurred and the polyacrylate is formed, the solvent is removed from the composition to produce a melt having a solvent content <2% by weight (column 6, lines 54-56). Hence, the teaching is that the solvent is not required for subsequent processing steps, because the polyacrylate composition is further processed as a melt, but it is essential in producing the polyacrylate.

This indicates that the monomer particles are not merely suspended in the solvent, acting merely as liquid phase, but that they are solubilized. More evidence for solubilization is provided at column 6, lines 30-34 where it states that:

> "A water-miscible or hydrophilic cosolvent may be added to the aqueous polymerization reactions in order to ensure that in the course of monomer conversion the reaction mixture is present in the form of a homogenous phase."

Because there is no basis for the assertion that the melt of Husemann is prepared by mixing two distinct particulates as recited in claim 1, the rejection of claims 1-4, 6-10, 29, and 30 is improper.

Finally, because claim 8 has been amended to recite the limitations of claim 12, which was not rejected over Husemann, the rejection of claims 8-10 should be withdrawn.

For all these reasons, the rejection of claims 1-4, 6-10, 29, 30 for obviousness over Husemann should be withdrawn.

The rejection of claims 17, 18, and 21 under 35 U.S.C. § 103(a) for obviousness over Schönwald in view of PCT Publication No. WO 03/094898 to Childs et al. ("Childs") is respectfully traversed.

Childs is cited for teaching biomedical applications of N-vinylpyrrolidone and optimum molar ratios of ionically cross-linkable polymeric material to ethylenically unsaturated molecules. However, Childs does not overcome the above-noted limitations of Schönwald. Therefore, the obviousness rejection of claims 17-18 and 21 is improper and should be withdrawn.

The rejection of claims 22 and 30 under 35 U.S.C. § 103(a) for obviousness over Schönwald is respectfully traversed.

According to the PTO, it would have been obvious to one of ordinary skill in the art at the time of the invention to optimize the formulation of the claimed invention as set forth in claims 22 and 30. This rejection is based on the PTO's position that Schönwald teaches or suggests all of the limitations of claim 1 (from which claims 22 and 30 depend). However, as noted above, Schönwald fails to teach or suggest all of the limitations of claim 1 and, therefore, cannot be said to render dependent claims 22 and 30 obvious. Therefore, this rejection is improper and should be withdrawn.

In view of all of the foregoing, it is submitted that this case is in condition for allowance and such allowance is earnestly solicited.

Respectfully submitted,

Date: March 7, 2009

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